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ENVIRONMENTAL TOBACCO SMOKE (ETS) AND CARDIOVASCULAR DISEASE

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ABSTRACT

The epidemiological evidence relating exposure to ETS and cardiovascular diseases has been examined: all of it is flawed. Most of the difficulties arise from the different study designs. Three of six studies report an increased RR for cardiovascular diseases, although the others failed to do so. It is concluded that no increased RR has been established unequivocally, either because there is none, or because the inadequate design of the studies frustrated their objective.

INTRODUCTION

Exposure to environmental tobacco smoke (ETS) has been associated with a number of serious diseases in man. In virtually all cases, it has not been possible to simulate in animal models the adverse health effects reported in man, so the evidence depends upon the findings of epidemiological studies. There is distinct weakness in the design of these studies, some of which are peculiar to the evaluation of effects of ETS (1), and others which are common to all epidemiological investigations (2). With respect to ETS, two factors prevent us reaching unambiguous answers; first, there is the poor assessment of the extent of exposure (3), and secondly, there is the misclassification of some cigarette smokers or ex-smokers as non-smokers (4).

In the report of the Surgeon General (5), less than 2 of 359 pages are dedicated to ETS and cardiovascular disease. In another comparable review, conducted by the New York Academy of Science (3), only 11 of 337 pages refer to cardiovascular diseases. The present paper considers six epidemiological studies identified in an extensive search of the literature (6-11).

The first thing to note from this database is that the majority of the studies were not designed specifically to investigate the effects of ETS exposure on the incidence of cardiovascular disease, but were adapted to this purpose from some other, once the initial claims that ETS affects health adversely had appeared in 1981-2 (see 12, 13). This adaptation of existing studies has led to effects being sought in populations that are not representative of the population at large.

How is exposure to ETS quantified? No substance is known that

is representative of all the components of ETS (3), so it is not possible to monitor such exposure in a meaningful manner. Instead, epidemiologists have to resort to some subjective index of exposure, usually in the form of the smoking behaviour of couples living together. In most studies, the incidence of a specific medical outcome is determined in a group of non-smokers married to cigarette smokers, and this rate is then compared with that in non-smokers married to non-smokers. In this way, exposure to ETS in the home can be assessed, although no allowance is made for exposure of both groups to ETS outside the home, or for any effects arising from exposure to other, potentially toxic, agents. It seems likely that any effects of ETS, if there are any, would be masked by the variability introduced by these confounding influences.

The smoking status of the participants in epidemiological studies is determined from questionnaires. The reliability of the answers to the questions that constitutes this part of the experimental design is low. It is inevitable that some subjects are misclassified with respect to their cigarette smoking behaviour; this probably results from simple failures in memory, or is the consequence of giving false answers to avoid admitting that they have a habit which is considered to be socially undesirable.

All the reports considered in this review have appeared since 1985, i.e. after the first suggestion in (1981) that exposure to ETS may be associated with serious health problems (12,13). However, the measurements on the subjects in the trials were made in the 1970s, i.e. retrospectively, and thus can be considered to be the result of data dredging.

REVIEW

The Garland et al study (8) was performed over a 10 year period after enrolment between 1972 and 1974 of 82% of the adults aged between 50 and 79 in a community of San Diego, in the U.S.A. In the period under consideration, there were 19 deaths from ischaemic heart disease (determined by analysis of death certificates). Only two deaths were recorded in the control group (non-smokers married to non-smokers), which probably represents too low a baseline level to permit safe predictions from these data to the population at large. The age-adjusted death rates for ischaemic heart disease were not significantly elevated in the subjects considered to be exposed to ETS ($P > 0.1$), and were higher in those married to ex-smokers than in those married to current smokers.

The investigation reported by Lee et al (11) was a case-control study initially designed to examine lung cancer risk. With respect to ischaemic heart disease, no statistically significant increased risk was associated with supposed exposure to ETS in the home, at work, or from travel and leisure.

Svendsen et al (9) selected a sub-group of patients for analysis from the cohort in the multiple risk factor intervention trial (MRFIT). MRFIT was designed to measure the effect of different interventions on mortality of patients identified as being at high risk of coronary heart disease. Men aged 35 to 57 years old were recruited in 18 cities in the U.S.A., and followed

for a mean time of seven years. The smoking status of the cohort was determined by questionnaire and, unusually for such studies, confirmed by objective measures (i.e. measurement of serum thiocyanate levels and exhaled carbon monoxide); the cause of death was determined by a committee of three cardiologists reviewing the case-papers on a blind basis (i.e. not aware of the treatment assignment, or, in this case, the spousal smoking status). There was a small apparent increased relative risk associated with exposure to ETS in the home, but this did not reach the level of statistical significance ($P > 0.05$ for all comparisons, except for death from any cause, when $P = 0.01$). This very carefully conducted investigation was characterised by the small size of the groups under consideration (controls 56 non-fatal and fatal events in 959 subjects; spouse smokers 26 events in 286 subjects), and the sub-group selected may have been atypical, because it was chosen from the highest 15% of those at risk from cardiovascular disease.

Helsing et al (7) considered a population of 91,909 white people from Washington County, Maryland, U.S.A. aged 25 or older on entry in July 1963. Smoking status was determined from responses made to a private census conducted in 1963, i.e. before the publication of the Surgeon General's first report in 1964 (14), and then allocated a score on the basis of the extent of smoking, whether or not it was current, and the type of tobacco consumed (cigarette, pipe or cigar). The population was followed for 12 years, with the cause of all deaths determined from death certificates. There were 2022 deaths from arteriosclerotic heart disease in non-smokers. The adjusted (for age, marital status, years of schooling and quality of housing) rates of death from arteriosclerotic heart disease of the population was then assessed with respect to exposure to ETS in the home; a statistically significant relative risk was detected for both men (1.31, 95% confidence limits 1.1-1.6) and women (1.24, 95% confidence limits 1.1-1.4). However, it was not possible to demonstrate any increase in risk with increased exposure in men, but there was such a relationship in women ($P < 0.005$).

The study of Helsing et al can be criticised in a number of ways. First, the smoking status of the subjects was determined once in 1963, so there was no possibility of allowing for any subsequent changes in behaviour. Secondly, there was no information on the established risk factors for the disease, such as blood pressure and serum cholesterol levels in the exposed and unexposed groups. Finally, the end-point used in the study relied on death certificates, which are prone to considerable inaccuracy (15).

The Gillis et al study (6, 16) was set up in 1972-76 in Renfrew and Paisley in an attempt to detect any special circumstances that may relate to the very high rates of lung cancer and cardiovascular disease that occur in the west of Scotland. Men and women between the ages of 46 and 64 were recruited and smoking behaviour determined from a self-administered questionnaire, and subsequently checked by an experienced interviewer when the subjects attended a screening centre. A cohort of 15399 subjects was identified (80% of those qualified to participate), and followed for an average of 11.5 years. Cause of death was determined from death certificates. From these data, it was

possible to calculate the relative risk associated with exposure to ETS in the home. The only statistically significant RR was for ischaemic heart disease in non-smokers (2.01, P = 0.008), which is a remarkably high value, because the RR from smoking was only 2.27. There were 30 deaths in the control group and 54 in those considered to be exposed to ETS in their homes. When cardiovascular symptoms were detected in the screening component of this study, there were no statistically significant differences between the exposed and unexposed groups with respect to angina and major abnormalities of the electrocardiogram. It is possible that the ischaemic heart disease mortality rate for those considered to be exposed to ETS represents a spurious finding, because of the absence of any effect on the pre-terminal cardiovascular symptoms, and because of the magnitude of the effect relative to that seen in smokers.

The final study in this database is the one from Japan, described by Hirayama (10). A prospective epidemiological study on a cohort of 265,118 Japanese people was initiated in 1966, with a view to determining the incidence of serious disease. The cause of death used as an end point in the investigation was taken from death certificates. This study led to the first suggestion that exposure to ETS was associated with an increased risk of lung cancer (13); further consideration has resulted in additional claims of adverse health effects due to spousal cigarette smoking, including a RR of 1.31 for ischaemic heart disease (P < 0.019) in non-smoking women in 1984 (17). This is a surprising finding, because a report three years earlier on the same cohort led to the conclusion that "passive smoking did not seem to increase the risk of developing ischaemic heart disease" (13).

The importance of Hirayama's various reports in the field of adverse health effects of ETS cannot be underestimated. Unfortunately, most of the influence has arisen from a poorly designed study, which has been much criticised, partly because of the unclear way it has been presented in the literature. The cohort was assembled as a convenient sample, rather than as a representative one, which has resulted in over-dependence on certain categories of the population at large, e.g. agricultural workers and young people (only 2% were over 60, whereas 12% of the Japanese population fall into this category). Japanese women spend much of their time in small rooms, where any effect of ETS would be greater than in the larger indoor air spaces frequented by those who live in the west. The cooking habits of the wives of Japanese agricultural workers may have confounded the study, because kerosene stoves would have been used extensively, and these are known to emit large quantities of potentially toxic gasses and particulate matter (18). The misclassification of smokers and ex-smokers of cigarettes as non-smokers may also have contributed to the empirical findings. No doubt the influence of many of these factors could have been taken into account in evaluating the validity of the results, but this has not been possible because Hirayama has refused to give other epidemiologists access to his data (19). Such secrecy does not inspire confidence in the objectivity of the conclusions reached in the Japanese study.

CONCLUSIONS

Of the six studies considered here, only three revealed any significant effects. Each of the positive studies was flawed in some way. Two consistent problems are apparent: too strong a reliance on the accuracy of death certificates, and the unreliability surrounding the determination of the smoking status of the subjects and their spouses in order to measure of exposure to ETS. It is concluded that no increased risk of cardiovascular disease can be associated unequivocally with exposure to ETS, and it seems probable that this will continue to be the case until specifically designed trials are instigated, and some objective measure of degree of exposure can be devised.

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